US Army Medical Research and Materiel

Technology Available for Licensing

Botulinum Neurotoxin Vaccine

This vaccine is an improved method and composition for inducing a protective immune response against four botulinum neurotoxin (BoNT) serotypes (A, B, C, and F). Studies of the other three serotypes (D, E, and G) are in progress. The sequences encoding nontoxic fragments of BoNT serotypes A - G have been inserted into a Venezuelan equine encephalitis (VEE) virus replicon. The resultant self-replicating RNA molecule makes abundant quantities of mRNA that encode the foreign proteins which in turn can be used as a vaccine.

Neurotoxins produced by *Clostridium botulinum* cause botulism by blocking the transmission of neuromuscular stimuli. The blockage results in neuromuscular weakness and flaccid paralysis, which can lead to respiratory failure and death. Humans are naturally infected by BoNT in three ways: food poisoning, infant botulism, and wound botulism. Ingestion of improperly prepared or canned foods has resulted in numerous cases of botulism. The current botulism vaccine is comprised of the complete toxoid. However, it is dangerous and expensive to produce and contains formalin, which causes reactogenic effects in vaccine recipients. It is also incomplete as it only protects against serotypes A – E and requires four inoculations over 12 months. A more effective vaccine is needed to protect humans against all seven BoNT serotypes as they are [illegible]cally distinct and do not cross protect.

Animal studies showed that VEE replicon particles (VRPs) expressing the serotypes A, B, C or F could immunize and protect an inbred and an outbred mouse strain from a lethal challenge of BoNT/A or BoNT/B, BoNT/C, or BoNT/F, respectively. The ability of VRPs expressing BoNT serotypes D, E, and G to protect animals is being investigated.

Features and advantages:

- **Uses the VEE replicon to express prokaryotic genes in eukaryotic cells**
- **Provides for easy purification of large quantities of protein product that are devoid of endotoxin**
- **Replicon vaccine improves immune response as genes are expressed in lymph nodes**
- **Vaccine stimulates mucosal immune responses**
- **VRPs are**
- **VRPs may be administered by parenteral injection or**

Patent Status

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